REMARKS

Claims 1-6, 8-9, 11-35, 38-39, 42-48 were pending in the application. Claims 11, 13, 20-35 and 39-44 are hereby cancelled without prejudice to pursuing the cancelled claims in this or other continuing applications. Claim 12 has been amended. The amendment is supported fully by the claims and/or specification as originally filed and, thus, do not represent new subject matter. Upon entry of these amendments, Claims 1-6, 8-9, 12, 14-19, 38, and 45-48 will be pending and under active consideration. Claims 1 and 12 are independent.

Claims 11, 13, 20-35 and 39-44 are cancelled herein without prejudice to pursuing the cancelled claims in this or other continuing applications. These claims are cancelled solely to advance the prosecution of the present application and without acquiescing in the propriety of the rejections presented against them.

Claim 12 has been amended to point out more particularly and claim more distinctly that which Applicants regard as their invention by now reciting "human hepatic progenitors," The amendment corrects previous typographical errors and is supported fully by the claims and/or specification as originally filed and, thus, does not represent new subject matter.

Applicants respectfully request entry of the amendments and remarks made herein into the file history of the present invention. Reconsideration and withdrawal of the rejections set forth in the above-identified Office Action are respectfully requested.

I. The Rejections Under 35 U.S.C. § 102 Should Be Withdrawn

A. The Rejections Over Muench *et al.* Under 35 U.S.C. § 102(b)

Amended Claims 21-23 and 42-44 are rejected in the Final Office Action, pages 14-15, under 35 U.S.C. § 102(b) as allegedly being anticipated by Muench *et al.* (*Blood,* 83:3170-3181, 1994)(hereinafter, "Muench '94") or Muench *et al.* (*Blood,* 89:1364-1375, 1997)(hereinafter, "Muench '97")(jointly, the "Muench References") for the reasons of record. In particular, the Final Office Action alleges that the human hepatic pluripotent progenitors of the presently claimed invention are indistinguishable over the isolated human fetal liver hemopoietic progenitor cell populations of the Muench References because both progenitors share the same common cell surface antigens. The Final Office Action concludes, therefore, that the Muench References allegedly anticipate Applicants' claimed invention. Further, the Final Office Action alleges, in its "Response to Arguments" made by Applicants in support of the amended claims in Applicants' Amendment of September 30, 2002, Paper No. 16, that the human hepatic pluripotent progenitors of the presently claimed invention comprise hemopoietic progenitors. Applicants traverse respectfully.

Without acquiescing in the propriety of the rejection, Applicants herein cancel Claims 21-23 and 42-44 without prejudice and solely to advance prosecution of the present application. Accordingly, Applicants submit respectfully that the instant rejection has been rendered moot, and Applicants request respectfully that the rejection of Claims 21-23 and 42-44 under 35 U.S.C. § 102(b) be withdrawn.

Nevertheless, for the record, Applicants submit respectfully that the hemopoietic progenitor cells of the Muench References are distinct and different from hepatic progenitor cells of the present invention as claimed. Respectfully, Applicants direct the Examiner's attention to

page 22, lines 3-7, of the specification which define "hepatic progenitors" as cells that "give rise to hepatocytes and biliary cells," including three subpopulations: "hepatic stem cells, committed hepatocytic progenitors, and committed biliary progenitors, the last two being immature cells that are descendants of the hepatic stem cell and that have a single fate, either hepatocytes or biliary cells, but not both." The definition of "stem cells" provided in the specification at page 21, lines 26-28, distinguishes hepatic stem cells as separate and distinct from hemopoietic stem cells in the recitation, "By contrast, determined stem cells, such as hemopoietic, neuronal, skin, **or** hepatic stem cells, are pluripotent and have extensive growth capacity ... ." (Emphasis added). Thus, Applicants submit respectfully that the Final Office Action's assertion that the claimed human hepatic pluripotent progenitors comprise hemopoietic progenitors is in error.

Further, Applicants submit respectfully that the claimed human hepatic pluripotent progenitors do not share **all of** the same common cell surface antigens with the human fetal liver hemopoietic progenitor cell populations of the Muench References. As noted in the Final Office Action in the paragraph bridging pages 14-15, Muench '94 discloses the isolation of human fetal liver progenitors with a phenotype of CD34+, CD33+, CD13+, **CD38-**, **lin$^-$** (lineage=CD3, CD8, CD10, **CD14**, CD15, CD16, CD19, CD20 and glycophorin A), CD45RA$^-$, CD45RO$^-$, CD71$^-$, and heterogeneous for *c-kit* or CD117; and further discloses the isolation of CD34$^+$, CD33$^-$, HLA-DR$^-$, **CD38$^-$** cell populations; and Muench '97 discloses the isolation of hematopoietic stem cells with a phenotype of CD4$^+$, CD34^{++}, **Lin$^-$** (**CD14$^-$**), CD117$^+$, **CD38$^-$**, and CD45RA. Respectfully, Applicants direct the Examiner's attention to the present specification, page 31, lines 9-12, which recites, "the inventors identify hepatic progenitor cells by sorting for those cells that strongly express alpha-fetoprotein, weakly express albumin, and express **CD14**, CD 34, **CD 38**, CD 117, or a combination thereof." Thus, whereas the Muench References disclose cells

that are **CD38$^-$** and **CD14$^-$**, Applicants' hepatic progenitor cells express a **CD14$^+$**, **CD 38$^+$** phenotype. Accordingly, Applicants submit respectfully that the Final Office Action's assertion that the claimed human hepatic pluripotent progenitors share the same common cell surface antigens with the human fetal liver hemopoietic progenitor cell populations of the Muench References is in error.

In view of the above, Applicants submit respectfully that Claims 21-23 and 42-44 are not anticipated by the Muench References. Further, inasmuch as Claims 21-23 and 42-44 have been cancelled herein, Applicants submit respectfully that the rejection under 35 U.S.C. § 102(b) has been rendered moot. Accordingly, Applicants request respectfully that the rejection of Claims 21-23 and 42-44 under 35 U.S.C. § 102(b) be withdrawn.

B. The Rejection Over Craig *et al.* Under 35 U.S.C. § 102(b)

The Final Office Action, at pages 16-17, rejects Claims 1-2, 4-6, 8-9, 11-14, 18-23, and 42-44 as allegedly being anticipated by Craig *et al.* (*J. Exp. Med.*, 17:1331-1342, 1993) (hereinafter, "Craig"), under 35 U.S.C. § 102(b). The Final Office Action alleges that the cell isolation method of Craig is indistinguishable from the method of the instant claims; therefore, the method of Craig allegedly inherently produces an enriched mixture of cells comprised of an enriched population of human liver progenitors and/or human hepatic progenitors as claimed. Moreover, the Final Office Action alleges that the human hepatic pluripotent progenitors of the presently claimed invention are indistinguishable over the isolated human fetal liver hemopoietic cell populations of Craig because they allegedly share the same common cell surface antigens and the human liver progenitors and/or hepatic pluripotent progenitors of the presently claimed invention comprise hemopoietic progenitors. Applicants traverse respectfully.

Without acquiescing in the propriety of the rejection, Applicants herein cancel Claims 20-23 and 42-44 without prejudice and solely to advance prosecution of the present application. Accordingly, Applicants submit respectfully that the instant rejection has been rendered moot, and Applicants request respectfully that the rejection of Claims 20-23 and 42-44 under 35 U.S.C. § 102(b) be withdrawn.

With regard to Claims 1-2, 4-6, 8-9, 11-14, and 18-19, and for the record with regard to Claims 20-23 and 42-44, Applicants submit respectfully that, as noted above, hemopoietic progenitor cells as described by Craig are distinct and different from hepatic progenitor cells of the present invention as claimed. Thus, Applicants submit respectfully that the Final Office Action's assertion that the claimed human hepatic pluripotent progenitors comprise hemopoietic progenitors is in error.

Moreover, Applicants submit respectfully that the claimed human hepatic pluripotent progenitors do not share the same pattern of expression of cell surface antigens with the human fetal liver hemopoietic progenitor cell populations of Craig. As noted in the Final Office Action at page 16, lines 4-5, Craig discloses the isolation of human hemopoietic progenitor cells with a phenotype of Thy-1^+, $CD34^+$, **$CD38^{low}$**, $CD45RA^-$, **$CD45RO^+$**, $CD71^{low}$ and **$CD117^{low}$**. As disclosed and claimed by Applicants, the instant hepatic progenitor cells express a $CD38^+$, $CD45^-$, $CD117^+$ phenotype. See, for example, Claims 43 and 44 and page 36, lines 25-28. Applicants submit respectfully that one skilled in the art will recognize that "low" expression is distinct and different from "+ expression." Hence, Applicants submit respectfully that the Final Office Action's assertion that the claimed human hepatic pluripotent progenitors share the same common cell surface antigens with the human fetal liver hemopoietic progenitor cell populations of Craig is in error.

The Final Office Action alleges that the method of Craig is indistinguishable from the method of the instant claims; the method of Craig allegedly inherently produces an enriched mixture of cells comprised of an enriched population of human liver progenitors and/or human heptatic progenitors as claimed. Respectfully, Applicants disagree. Without acquiescing in the Final Office Action's allegation that the Ficoll-Paque density centrifugation taught by Craig anticipates the debulking step of Applicants' claimed method, Applicants submit respectfully that the immunoselection procedure disclosed by Craig cannot be practiced to arrive at the instant hepatic progenitor cells. In fact, the practice of Craig's method selects ***against*** the hepatic progenitor cells claimed by Applicants in at least two aspects.

First, the guiding force of Craig's disclosure is the selective power of the anti-Thy-1 antibody in isolating hemopoietic progenitor cells; Craig selects for Thy-1 expression in every case. However, at page 1336, first column, lines 15-17, Craig teaches that "Thy-1 staining was highest on $CD38^-CD34^+$ cells, and decreased with increased CD38 expression." Applicants' claimed hepatic progenitors express CD38 in all cases, and strongly or very strongly in some cases. See, for example, Claims 43 and 44 and page 36, lines 25-28. Hence, Craig's method works in ***opposition*** to the isolation of Applicants' claimed hepatic progenitors.

Second, Craig notes at page 1338, column 1, lines 14-19, with regard to the $CD45RA^-$ and $CD45RO^+$ expression data in cells isolated by Craig's method, that "the lack of CD45RA expression on the majority of FL[fetal liver] $CD34^+$ cells examined coincides with expression of CD45RO ... and underscores the importance of CD45 isoform expression in the differentiation of hematopoietic cells." Stated another way, Craig is disclosing that CD45 expression (of one isoform or another) is fundamental to the types of cells Craig's method is intended to isolate; *i.e.*, hemopoietic progenitor cells. This point is echoed by Applicants at page 65, lines 6-14,

particularly lines 9-10, which recite, "cells exhibiting CD45, which is expressed on all mature hemopoietic cells," are removed via immunoselection if selection of hepatic progenitors of the present invention is intended. Applicants submit respectfully that the CD45 antigen is disclosed by Applicants, for example at page 27, line 27, or at page 29, line 26, as being an antigen useful in selecting ***against*** the hepatic progenitor cells of the present invention, contrary to the teaching of Craig. Hence, Craig's method actually teaches away from isolating the claimed hepatic progenitor cells.

Furthermore, Craig does not disclose immunoselection based on alpha-fetoprotein expression, which Applicants disclose as being very high in the instant hepatic progenitor cells (see page 36, line 29), albumin expression, or CD14 expression, also disclosed by Applicants for the selection of the instant hepatic progenitor cells (see page 36, lines 1 and 26 and Claim 12, for example). Thus, Applicants submit respectfully that Craig's method is **not** indistinguishable from Applicants' claimed method as alleged in the Final Office Action.

As Examiner is no doubt well aware, each and every element of the instant claims, as amended, must be disclosed by an allegedly anticipatory reference, either explicitly or inherently, for a *prima facie* showing of anticipation. Applicants submit respectfully that Craig fails to disclose each and every element of Applicants' Claims 1-2, 4-6, 8-9, 11-14, and 18-19, as amended. Accordingly, Applicants submit respectfully that the rejection of the claims of the present invention, as amended, is either rendered moot or claims 1-2, 4-6, 8-9, 11-14, and 18-19 are not anticipated by Craig. Applicants request respectfully that the rejections to Claims 1-2, 4-6, 8-9, 11-14,18-23, and 42-44 under 35 U.S.C. § 102(b) be withdrawn.

C. The Rejection Over Faris Under 35 U.S.C. § 102(e)

The Final Office Action, at pages 17-18, rejects Claims 11, 20, 21-26 and 42-44 under 35 U.S.C. § 102(e) as allegedly being anticipated by U.S. Patent No. 6,129,911 to Faris (hereinafter, "Faris"). The Final Office Action alleges that Faris teaches the preparation and isolation of a liver cell cluster of less than 10 cells comprising a liver stem cell and a hepatocyte, and a primary liver stem cell derived from human liver tissue, in which said stem cell comprises DNA encoding a heterologous polypeptide, such as ornithine transcarbamylase, glutam me synthetase, Factor XIII, Factor IX and others. The Final Office Action alleges further that the primary liver stem cell derived from human liver tissue is defined as undifferentiated cell that differentiates into a mature functional hepatocyte or bile duct cell which is allegedly consistent with the definition of hepatic progenitors of the instant claimed invention. The Final Office Action concludes that, since a product and its properties can not be separated, the composition of isolated liver cell cluster of Faris is the same as the enriched population of human hepatic pluripotent progenitors of the instant invention regardless of how they are isolated and, therefore, the reference allegedly anticipates the instant claims. Applicants traverse respectfully.

Without acquiescing in the propriety of the rejection based on Faris, Applicants herein cancel Claims 1, 20, 21-26 and 42-44, without prejudice. Accordingly, Applicants submit respectfully that the instant rejection has been rendered moot, and Applicants request respectfully that the rejection of Claims 11, 20, 21-26 and 42-44 under 35 U.S.C. § 102(e) be withdrawn.

II. The Rejections Under 35 U.S.C. § 103(a) Should Be Withdrawn

A. The Rejection Over Reid In View Of Mitaka And Naughton

The Final Office Action, at pages 19-21, rejects Claims 1-6, 8, 12-19 and 45-48 under 35 U.S.C. § 103(a) as being allegedly obvious over U.S. Patent No. 6,069,005 to Reid *et al.* (hereinafter, "Reid") in view of Mitaka *et al.* (Biochem. Biophys. Res. Comm. 214:310-317, 1997)(hereinafter, "Mitaka") and U.S. Patent No. 5,559,022 to Naughton *et al.* (hereinafter, "Naughton"). The Final Office Action alleges that Reid teaches a method of isolating hepatic progenitors from rat fetal liver that express alpha-fetoprotein and albumin as claimed by Applicants. While the Final Office Action acknowledges that Reid is deficient in that it does not teach that the method is useful for isolating human liver cells, the Office Action alleges that Naughton cures this deficiency by teaching an isolation of liver progenitors from human liver. The Final Office Action also acknowledges that Reid is deficient in that Reid also fails to teach a step for debulking the cell suspension based on size, buoyant density, or a combination. However, the Final Office Action alleges that Mitaka cures this deficiency by teaching a an isolation of liver progenitors including a low speed centrifugation step. Applicants traverse respectfully.

In admitting that Reid teaches a method of isolating hepatic progenitors from rat fetal liver but is deficient with respect to teaching a step for debulking the cell suspension based on size, buoyant density, or a combination as claimed in the present application, the Final Office Action alleges that Mitaka cures the deficiencies of Reid by teaching the use of a low-speed centrifugation to separate mature hepatocytes from progenitor cells. Without acquiescing in the propriety of the allegation that Reid teaches such a method, Applicants submit respectfully that Reid may not be permissibly combined with Mitaka because Reid teaches away from the use of a

low-speed centrifugation step. A prior art reference must be considered in its entirety, *i.e.*, as a whole, including portions that would lead away from the claimed invention. *W.L. Gore & Associates, Inc. v. Garlock, Inc.*, 721 F.2d 1540, 220 USPQ 303 (Fed. Cir. 1983), cert. denied, 469 U.S. 851 (1984). It is improper to combine references where the references teach away from their combination. *In re Grasselli,* 713 F.2d 731, 743, 218 USPQ 769, 779 (Fed. Cir. 1983). A *prima facie* case of obviousness may also be rebutted by showing that the art, in any material respect, teaches away from the claimed invention. *In re Geisler*, 116 F.3d 1465, 1471, 43 USPQ2d 1362, 1366 (Fed. Cir. 1997).

Applicants submit respectfully that Reid teaches that low speed centrifugation is inimical to Reid's method of isolating hepatoblasts. For example, at column 4, lines 12-15, Reid recites "methods for isolation of hepatoblasts [that] require the use of fractionation for cell size or cell density ... are inadequate for separating the hemopoietic from the hepatopoietic precursors. ... Hence, currently available isolation methods have proven very inefficient." This teaching away is even more pronounced at column 19, lines 19-40. For example, lines 19-22 recite "[T]he advantage of this protocol in comparison with previous methods which involved ... low-speed differential centrifugation ... are several-fold." Applicants submit respectfully that one skilled in the art would be dissuaded from adding such a centrifugation step when Reid teaches that centrifugation is an inferior process. In fact, in view of Mitaka, the use of centrifugation in the method of Reid would result in *diminished recovery* of hepatocyte precursors. At column 19, lines 27-28, Reid teaches that "[D]issociated fetal hepatoblasts also readily form large aggregates." In a centrifugation step as described by Mitaka, large aggregates are found in the pellet fraction. Thus, using a centrifugation step as described by Mitaka, wherein the pellet is discarded and the supernatant is retained, the hepatoblasts that Reid's method isolates would be

thrown away! Accordingly, Applicants submit respectfully that Reid effectively teaches away from a combination with Mitaka.

Even further, although the Final Office Action alleges that "one of ordinary skilled artisan would have been motivated to further introduce a low speed centrifugation step in the modified isolation procedure to remove the bulk of large mature hepatocytes or parenchymal cells from progenitor cell populations," Reid indicates that Reid's methods for isolating hepatic precursors (*i.e.*, panning and flow cytometry) are sufficient without further steps. For example, Reid recites at column 6, lines 54-57, that "[T]he combination of the rapid panning methodology with the accuracy of the fluorescence activated cell sorting results in highly purified cell populations with good viability." Thus, one skilled in the art would have little motivation to add a low-speed centrifugation to the method of Reid as Reid teaches that such a step is unnecessary.

In point of fact, and as the Examiner is no doubt well aware, 35 U.S.C. § 103(a) obviousness can only be established by combining or modifying the teachings of the prior art to produce the claimed invention where there is some teaching, suggestion, or motivation to do so found either in the references themselves. "It is impermissible to reconstruct the claimed invention from selected pieces of prior art absent some suggestion, teaching, or motivation in the prior art to do so. " *Uniroyal, Inc. v. Rudkin-Wiley Corp.*, 837 F.2d 1044, 1051-2, 5 USPQ2d 1434, 1438 (Fed. Cir. 1988). As noted above, the Final Office Action alleges that it would have been obvious to one having ordinary skill in the art at the time the invention was made to modify the method of Reid with the centrifugation step of Mitaka in order to remove the bulk of large mature hepatocytes or parenchymal cells from progenitor cell populations. However, as further noted above, Applicants' careful reading of Reid reveals no motivation whatsoever with regard to the use such a centrifugation step.

Applicants submit respectfully that the requisite motivation to combine Mitaka's low-speed centrifugation into Reid's method of isolating hepatic progenitors is not present in the references themselves or in the knowledge generally available to one of ordinary skill in the art at the time of invention of Applicants' claimed invention. Applicants submit respectfully that the Final Office Action makes the assertion that the combination of Reid with Mitaka and Naughton would have been obvious to one skilled in the art without citation or recitation from the references to indicate the source of that teaching, suggestion, or motivation necessary to combine the references. Applicants request respectfully that, if this rejection is to be maintained, Examiner please kindly provide Applicants the source of the teaching, suggestion, or motivation to combine the references, as Applicants' own careful reading of the references does not reveal any such teaching, suggestion, or motivation to combine same. Absent such teaching, suggestion, or motivation found within the references, it cannot be inferred that Applicants' invention would have been obvious to one of ordinary skill in the art.

The Final Office Action alleges that it would have been obvious to one having ordinary skill in the art at the time the invention was made to modify the method of Reid with the centrifugation step of Mitaka in order to remove the bulk of large mature hepatocytes or parenchymal cells from progenitor cell populations, and that it also would have been obvious to provide Naughton's use of human liver into Reid's method in order to obtain a population of human liver progenitors. Thus, the only rationale provided in the Final Office Action for combining the references is "to obtain a composition enriched in a population of human liver progenitors or human hepatic pluripotent progenitors for cellular characterization as well as for cell transplantation studies ... [and] to remove the bulk of large mature hepatocytes or parenchymal cells from progenitor cell populations (5-15 micron in diameter), so that less

contaminating large sized parenchymal cells are present in the cell suspension subjected to panning and fluorescence activated cell sorting procedures"; *i.e.*, to reach the same result found in Applicants' claimed invention. Respectfully, Applicants ask, why would one skilled in the art, other than through a desire to recreate Applicants' claimed invention in retrospect, combine the references as suggested by the Final Office Action, above. Applicants respectfully remind the Examiner that "[I]t is insufficient to select from the prior art the separate components of the inventor's combination, using the blueprint supplied by the inventor." *Interconnect Planning Corp. v. Feil,* 774 F.2d 1132, 1143, 227 USPQ2d 543, 551 (Fed. Cir. 1985).

Thus, Applicants submit respectfully that the combination of Reid with Mitaka and Naughton, as suggested in the Office Action, to reach Applicants' claimed invention is impermissible under standard patent practice. Therefore, without acquiescing in the propriety of the rejection, Applicants submit respectfully that the combination of Reid with Mitaka and Naughton fails to meet the threshold required for establishing a *prima facie* case of obviousness under 35 U.S.C. § 103(a). Accordingly, Applicants request respectfully that the U.S.C. § 103(a) rejection of Claims 1-6, 8, 12-19, and 45-48 be withdrawn.

Furthermore, without acquiescing in the propriety of the rejection with regard to Claim 13, Applicants cancel Claim 13 herein without prejudice and solely to advance prosecution of the present application. Applicants submit respectfully that the instant rejection of Claim 13 is rendered moot.

Accordingly, Applicants submit respectfully that the rejection of Claims 1-6, 8, 12-19 and 45-48 under 35 U.S.C. § 103(a) has been overcome or rendered moot, and Applicants request respectfully that the rejection of Claims 1-6, 8, 12-19 and 45-48 under 35 U.S.C. § 103(a) be withdrawn.

B. The Rejection Over The Muench References In View Of Reid

The Final Office Action, at pages 22-24, reject Claims 21 and 38 as being allegedly obvious over the Muench References in view of Reid under 35 U.S.C. § 103(a) for the reasons of record. In sum, the Final Office Action alleges that the Muench References disclose the cell populations of Applicants' claimed invention, but acknowledges that the Muench References do not did not teach a cell culture comprising these cell populations, an extracellular matrix component, and a culture medium. The Final Office Action alleges that Reid cures this deficiency. Applicants traverse respectfully.

With regard to Claim 21, without acquiescing in the propriety of the rejection with regard to Claim 21, Applicants cancel Claim 21 herein without prejudice and solely to advance prosecution of the present application. Applicants submit respectfully that the instant rejection of Claim 21 is rendered moot.

With regard to Claim 38, and for the record with regard to Claim 21, Applicants submit respectfully that the combination of the Muench References with Reid does not render Claims 21 and 38 obvious under 35 U.S.C. § 103(a). As noted above, the Muench References fail to disclose the cell populations of the present invention as claimed; the Muench References disclose cells having different cell surface markers from those of the cells of the present invention. Without acquiescing in the propriety of the argument that Reid cures the deficiency of the Muench References, that they do not did not teach a cell culture comprising these cell populations, an extracellular matrix component, and a culture medium, Applicants submit respectfully that Reid does not cure, and is not alleged to cure, the deficiency in the Muench References with regard to the cell surface markers of Applicants' claimed inventive cells.

Accordingly, Applicants submit respectfully that the Muench References, taken alone or together or in combination with Reid, do not teach or suggest the cells and cells populations of Applicants' claimed invention.

In view of the above, Applicants request respectfully that the 35 U.S.C. § 103(a) rejection of Claims 21 and 38 be withdrawn.

III. The Rejection Under 35 U.S.C. § 112, First Paragraph

At pages 1-12 of the Final Office Action, Claims 27-35 and 39 are rejected under 35 U.S.C. § 112, first paragraph, as allegedly containing subject matter which was not described in the specification in such a way as to enable one skilled in the art to make and/or use the invention, for the reasons of record. The reasons of record, in sum, allege that gene therapy was not well enough developed in the art at the time of the filing of the present application to support the breadth of the present claims when considered in conjunction with the disclosure of the present specification. Applicants traverse respectfully.

Without acquiescing in the propriety of rejection, without prejudice to pursuing the cancelled subject matter in this or other applications, and solely to advance prosecution of the present application, Claims 27-35 and 39 are cancelled herein. Accordingly, Applicants submit respectfully that the rejection has been rendered moot, and Applicants request respectfully that the 35 U.S.C. § 112, first paragraph, rejection of Claims 27-35 and 39 be withdrawn.

IV. The Rejections Under 35 U.S.C. § 112, Second Paragraph

At pages 12-13 of the Final Office Action, Claims 11-20 and 44 are rejected under 35 U.S.C. § 112, second paragraph, as allegedly being indefinite for failing to point out particularly and claim distinctly the subject matter regarded as the invention. The Final Office Action alleges that, in claim 11, the phrase "A human hepatic pluripotent progenitor isolated by the method of claim 1" is unclear, because the method of Claim 1 provides a mixture of immature cells comprised of an enriched population of human liver progenitors, but the method allegedly does not recite any essential steps required to obtain a human hepatic pluripotent progenitor from a mixture of immature cells. The Final Office Action concludes, therefore, that it is allegedly unclear how a human hepatic pluripotent progenitor could be isolated or obtained from such a method. Applicants traverse respectfully.

Without acquiescing in the propriety of rejection, without prejudice to pursuing the cancelled subject matter in this or other applications, and solely to advance prosecution of the present application, Claims 11, 20, and 44 are cancelled herein. Accordingly, Applicants submit respectfully that the rejection has been rendered moot, and Applicants request respectfully that the 35 U.S.C. § 112, second paragraph, rejection of Claims 11, 20, and 44 be withdrawn.

The Final Office Action alleges that, in Claim 12 and its dependent claims, it is unclear what is the nexus of obtaining a mixture of cells which is comprised of an enriched population of human liver progenitors in step (c) with the preparation of a composition comprising an enriched population of human hepatic progenitors recited in the preamble of the claim. Clarification was requested because the metes and bounds of the claims are allegedly not clearly determined. Applicants traverse respectfully.

Without acquiescing in the propriety of the rejection, and solely to advance prosecution of the present application, Applicants amend Claim 12 to recite "human hepatic progenitors" rather than "human liver progenitors." Accordingly, Applicants submit respectfully that no lack of nexus now exists between the preamble and body of Claim 12 and its dependent claims. Applicants request respectfully that the rejection of Claim 12 and its dependent claims be withdrawn.

The Final Office Action notes that Claim 14 and its dependent claims recite the limitation "the immunoselection" in line 1 of Claim 14, and alleges that there is insufficient antecedent basis for this limitation in the claim because there is allegedly no recitation of any immunoselection step in the amended Claim 12 from which Claim 14 depends. Applicants traverse respectfully.

Respectfully, Applicants draw the Examiner's attention to line 1 of step (c) in Claim 12, wherein exists the recitation "subjecting the debulked suspension to a positive or negative immunoselection." Accordingly, Applicants submit that antecedent basis does, in fact, exist for the limitation "the immunoselection" in line 1 of Claim 14. Applicants request respectfully that the rejection of Claim 14 and its dependent claims be withdrawn.

On the basis of the foregoing, Applicants suggest respectfully that the rejections have been overcome, and Applicants request respectfully that the 35 U.S.C. § 112, second paragraph, rejection of Claims 11-20 and 44 be withdrawn.

IV. The Double Patenting Rejections Should Be Withdrawn

The Final Office Action provisionally rejects Claims 27-33 under the judicially created doctrine of obviousness-type double patenting as being allegedly unpatentable over

Claims 59-77 of copending Application No. 09/154,224. Although the conflicting claims are not identical, the Final Office Action alleges that they are not patentably distinct from each other because the instant claims encompass all the embodiments of the pending claims of the co-pending Application No. 09/154,224. Further, the Final Office Action provisionally rejects Claim 35 under the judicially created doctrine of obviousness-type double patenting as being unpatentable over Claims 21-39 of copending Application No. 09/534,487. The Examiner noted that Applicants will consider the possibility and propriety of filing a terminal disclaimer upon the allowance of the '224 Application or upon the allowance of '487 Application. Applicants traverse respectfully.

Inasmuch as Claims 27-33 and 35 are cancelled herein, as noted above, Applicants submit respectfully that the rejection has been rendered moot, and Applicants request respectfully that the doctrine of obviousness-type double patenting rejection of Claims 27-33 and 35 be withdrawn.

CONCLUSION

Applicants submit respectfully that the present application is in condition for allowance. Favorable reconsideration, withdrawal of the rejections set forth in the above-noted Office Action, and an early Notice of Allowance are requested.

Applicants' undersigned attorney may be reached in our Washington, D.C. office by telephone at (202) 625-3500. All correspondence should be directed to our address given below.

AUTHORIZATION

Applicants believe there is no fee due in connection with this filing. However, to the extent required, the Commissioner is hereby authorized to charge any fees due in connection with this filing to Deposit Account 50-1710 or credit any overpayment to same.

Respectfully submitted,

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